US006632192B2

(12) **United States Patent**
Gorsuch et al.

(10) **Patent No.: US 6,632,192 B2**
(45) **Date of Patent: Oct. 14, 2003**

(54) **APPARATUS AND METHOD FOR SELECTIVE REDUCTION OF SEGMENTAL INTRACELLULAR AND EXTRACELLULAR EDEMA**

(75) Inventors: **Reynolds G. Gorsuch**, Yountville, CA (US); **Kris Venkat**, Somerset, NJ (US)

(73) Assignee: **Transvivo, Inc.**, Napa, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 39 days.

(21) Appl. No.: **09/799,466**

(22) Filed: **Mar. 5, 2001**

(65) **Prior Publication Data**

US 2002/0123712 A1 Sep. 5, 2002

(51) **Int. Cl.**[7] **A61M 37/00**; A61M 5/00

(52) **U.S. Cl.** **604/6.04**; 604/6.09; 604/6.11; 604/9

(58) **Field of Search** 604/4.01, 5.01, 604/28, 506, 507, 29, 27, 6.09, 9, 6.01, 6.11, 6.12, 6.04, 5.04; 210/646

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,411,792 A 10/1983 Babb 210/651
4,950,224 A 8/1990 Gorsuch et al.
5,055,198 A * 10/1991 Shettigar 210/104
5,151,082 A 9/1992 Gorsuch et al.
5,152,743 A 10/1992 Gorsuch et al.
5,224,926 A 7/1993 Gorsuch et al.
5,242,382 A 9/1993 Gorsuch et al.
5,391,143 A * 2/1995 Kensey 604/28
5,735,809 A 4/1998 Gorsuch
5,744,031 A * 4/1998 Bene 210/143
5,968,004 A 10/1999 Gorsuch
5,980,478 A 11/1999 Gorsuch et al.
5,980,481 A 11/1999 Gorsuch
6,071,423 A * 6/2000 Brown et al. 210/782
6,200,485 B1 * 3/2001 Kitaevich et al. 210/134
6,287,516 B1 * 9/2001 Matson et al. 210/650

FOREIGN PATENT DOCUMENTS

EP 0 274 178 A1 7/1988

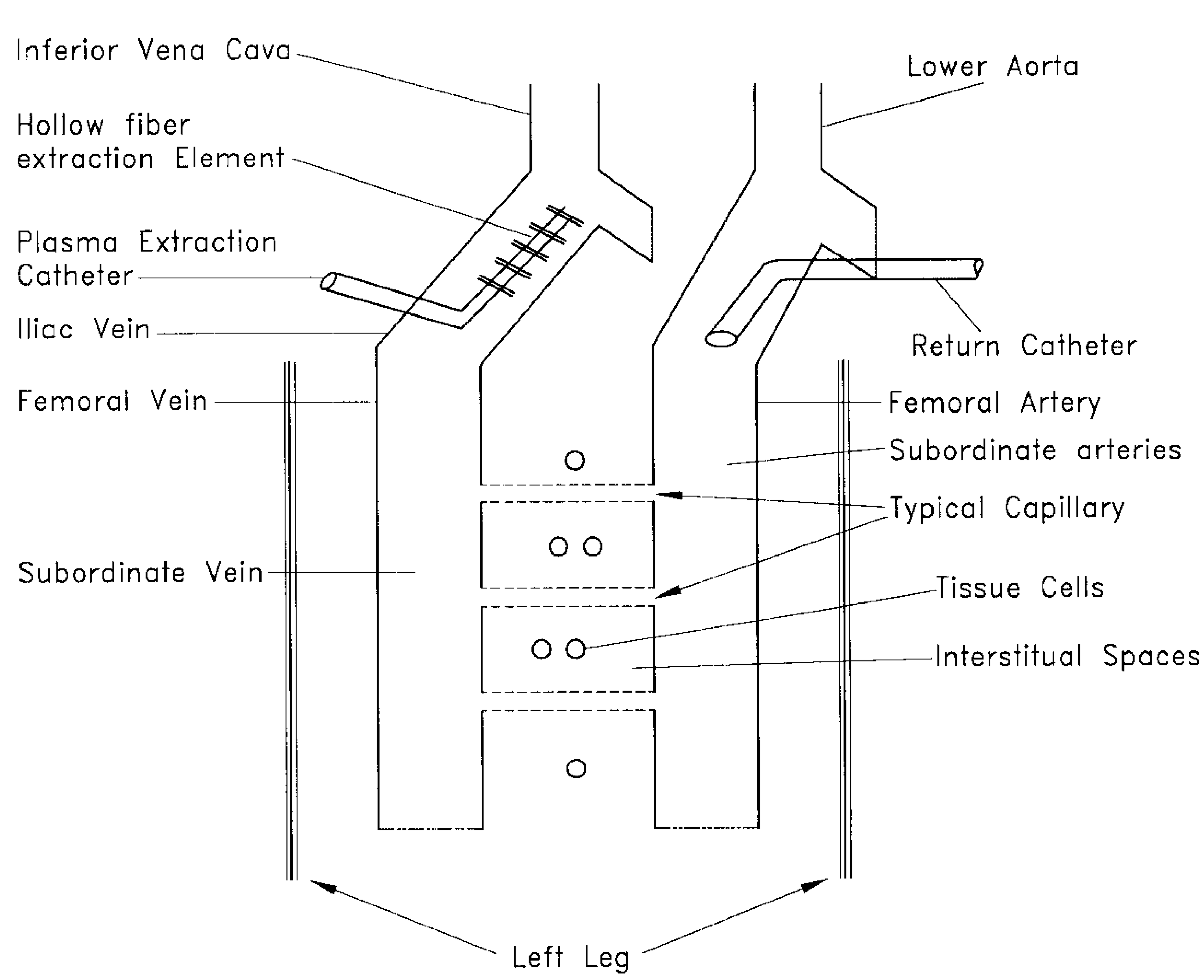
* cited by examiner

Primary Examiner—Angela D. Sykes
Assistant Examiner—Leslie R. Deak
(74) *Attorney, Agent, or Firm*—Knobbe, Martens, Olson & Bear LLP

(57) **ABSTRACT**

Segmental edema is treated by inserting a plasma extraction filter device in a major vein of a body segment or servicing the body segment containing the edemic tissues, and inserting a return catheter in a major artery of the body segment affected or feeding the body segment from which plasma is extracted. Blood plasma and plasma proteins extracted from the edemic body segment through the plasma extraction filter fluids are directed to an ultrafiltration apparatus where plasma water is separated from the plasma proteins. Plasma proteins are returned to the body segment from which the plasma was extracted via the return catheter in the major artery of the subject body segment.

18 Claims, 3 Drawing Sheets



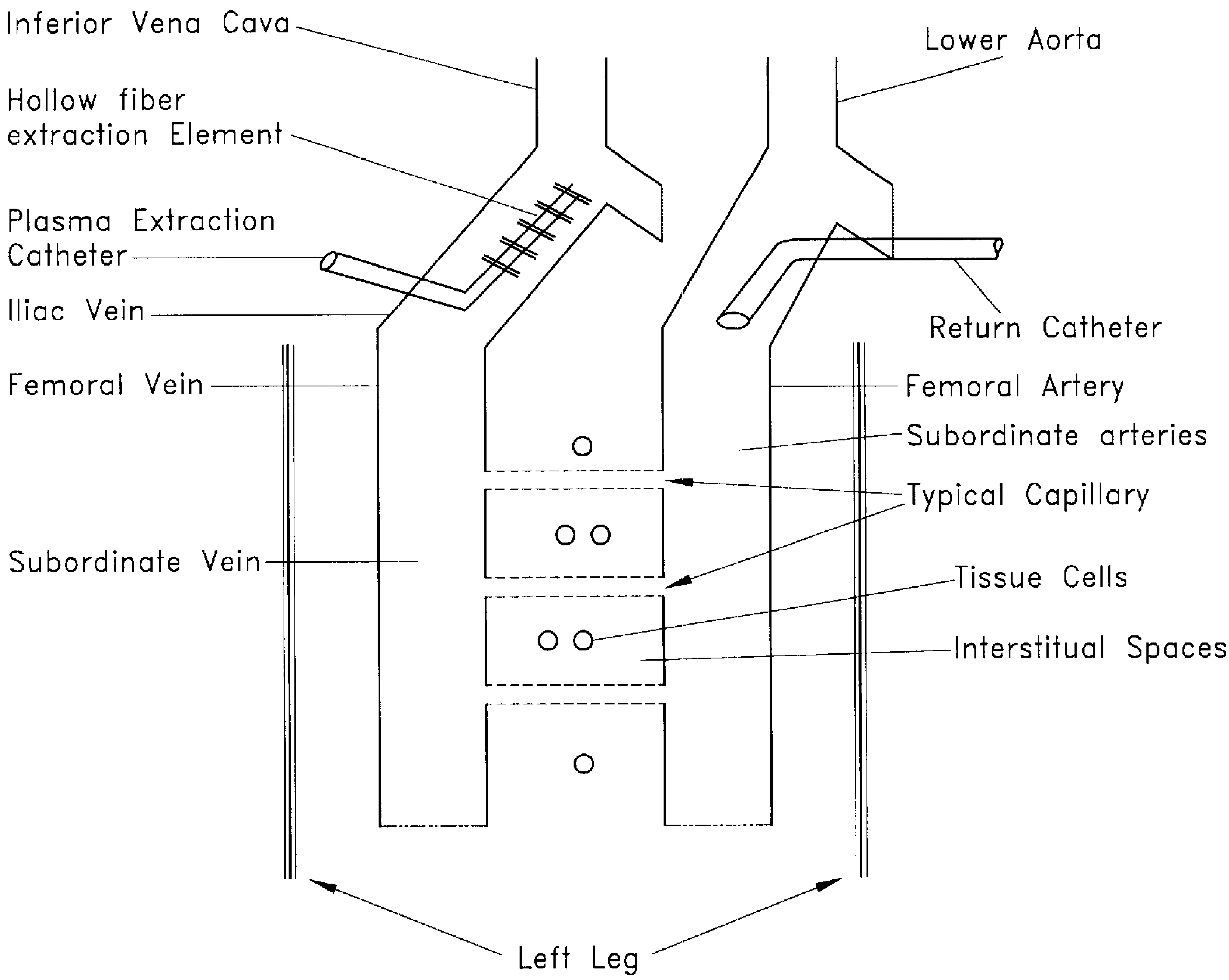
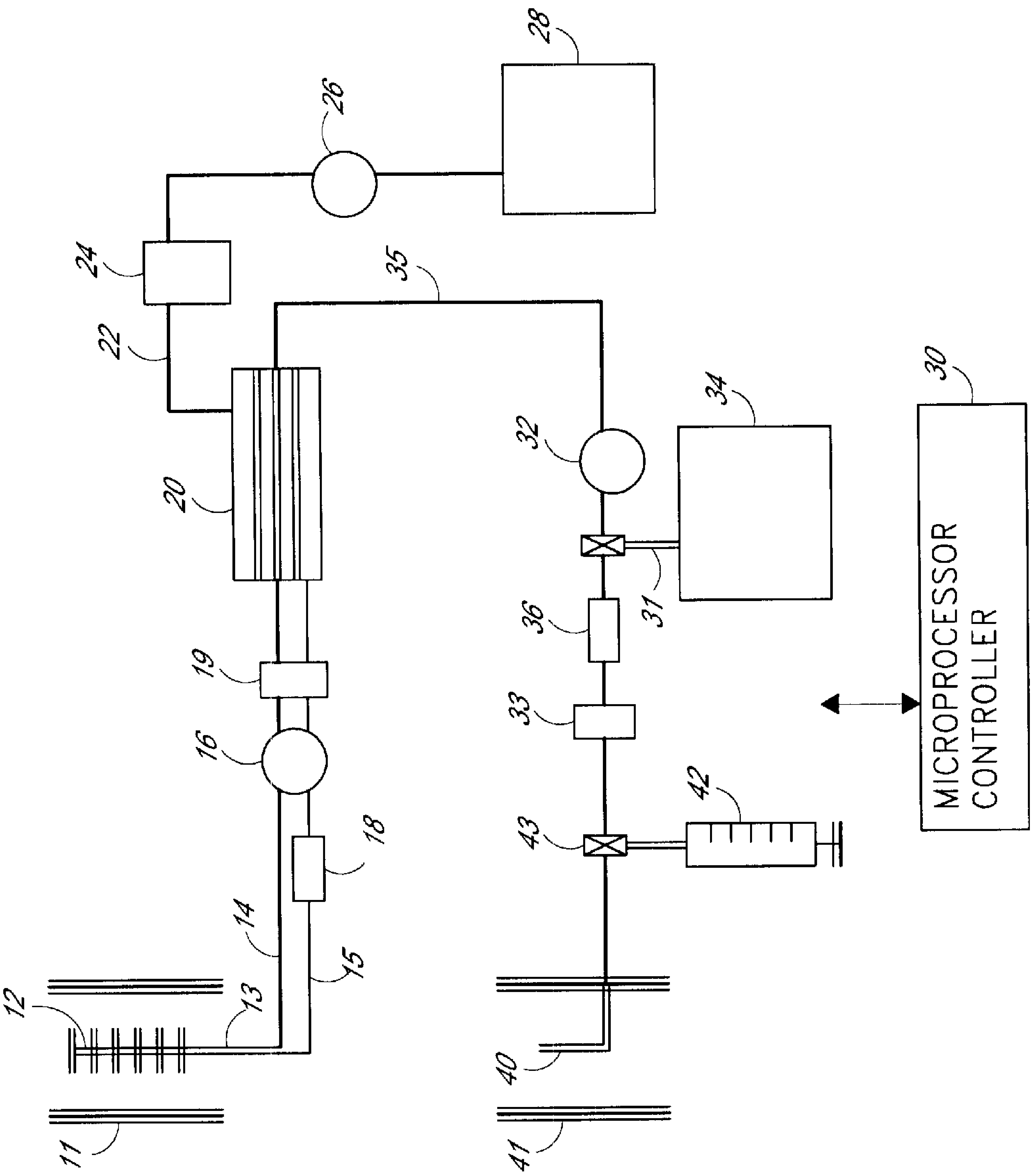

Inferior Vena Cava
Lower Aorta
Hollow fiber extraction Element
Plasma Extraction Catheter
Iliac Vein
Return Catheter
Femoral Vein
Femoral Artery
Subordinate arteries
Typical Capillary
Subordinate Vein
Tissue Cells
Interstitual Spaces
Left Leg

FIG. 1

FIG. 2


11
12
13
14
15
16
18
19
20
22
24
26
28
30
31
32
33
34
35
36
40
41
42
43
MICROPROCESSOR
CONTROLLER

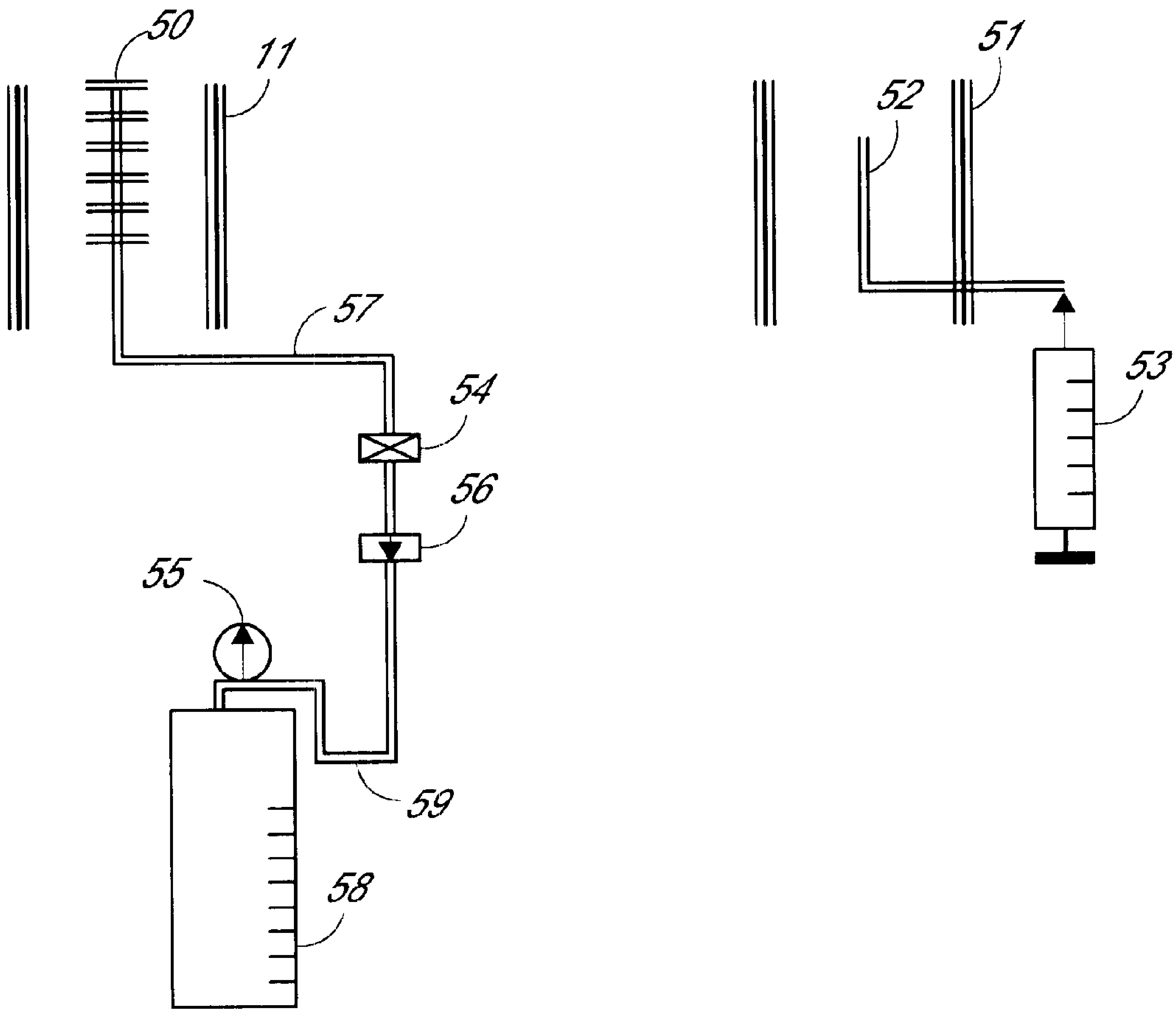


FIG. 3

APPARATUS AND METHOD FOR SELECTIVE REDUCTION OF SEGMENTAL INTRACELLULAR AND EXTRACELLULAR EDEMA

BACKGROUND OF THE INVENTION

Edema, by definition, is the presence of excess fluid in body tissue. An adult male weighing 70 kilograms is composed of about 50% fluid, nominally water, amounting to about 40 liters, approximately 25 liters of which is intracellular and about 15 liters extracellular. Edema occurs in both extracellular fluid compartments as well as intracellular fluid spaces. Although there are many causes of edema, the two most prevalent are heart failure and kidney disease nephrosis in which generalized systemic edema causes pulmonary failure with acute respiratory distress syndrome, and simultaneous pre-renal acute kidney failure. Fluid management systems for addressing such specific systemic conditions have been developed utilizing techniques and apparatus disclosed in U.S. Pat. Nos. 4,950,224, 5,151,082, 5,152,743, 5,224,926, 5,242,382, 5,735,809, 5,968,004, 5,980,478 and 5,980,481. The disclosures of the aforesaid patents are incorporated herein by reference.

A number of edemic conditions, although not systemic, occur in segmented sections of the body. For example, "Elephantitus" occurs when the lymph nodes in the lower extremities are blocked by infection, especially filarial nematodes resulting in localized edema. Blockage of lymph nodes by cancer, e.g., breast cancer, causes localized edema. Vascular bi-pass procedures can also induce severe localized edema. For treating such localized edema, it is far more preferable and proficient to treat the segment of the body affected rather than attempting to reduce systemic edema of the entire body which could result in negative side effects. However, current therapeutic methods for treating segmental edema involve complex physical therapy utilizing a modality of repeated massage techniques designed to enlist parallel lymphatic paths to relieve blocked lymph circulation. Such techniques are somewhat empirical in nature and have great variation in efficacy. These therapies also are used with special compression garments and/or bandages which must be continuously adjusted over time to fit changing needs of the patient. Oral and topical drugs such as Benzopyrones are often combined with the aforesaid therapeutic methods, resulting in long-term treatment, often six months to years before significant results are achieved.

SUMMARY OF THE INVENTION

The present invention is directed to means for the selective reduction of localized edemas in substantially reduced time for palliative results. The method of treating segmental edema according to the present invention comprises inserting a plasma extraction filter device in a major vein of a body segment or servicing the body segment containing the edemic tissues, and inserting a return catheter in a major artery of the body segment affected or feeding the body segment from which plasma is extracted. Blood plasma and plasma proteins extracted from the edemic body segment through the plasma extraction filter are directed to an ultrafiltration apparatus where plasma water is separated from the plasma proteins. Plasma proteins are returned to the body segment from which the plasma was extracted via the return catheter in the major artery of the subject body segment. Additional steps and techniques as well as the apparatus used for carrying out the method of the invention will be disclosed in further detail hereinafter.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a schematic drawing illustrating a typical body segment (left leg) including anatomical structure and placement of a plasma extraction catheter in an appropriate vein and a return catheter in an artery serving the affected body segment;

FIG. **2** is a schematic illustration of the plasma extraction and treatment apparatus of the invention; and

FIG. **3** schematically illustrates another more simplified embodiment of the invention using ultrafiltration membranes.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring to FIG. **1**, a left leg is schematically illustrated with the iliac and femoral veins extending into a patient's leg from the inferior vena cava, which leg is also fed by the femoral artery extending from the lower aorta. The illustration of the leg also shows subordinate arteries, typical capillaries, tissue cells and interstitial spaces which are affected by the segmented body portion or body segment treatment according to the invention. Localized fluid transfer between the capillaries and interstitial spaces is affected by the differential fluid pressure of the local capillary and interstitial spaces as well as the local plasma colloid osmotic pressure and interstitial colloid osmotic pressure differential. The colloid osmotic pressure in extracellular fluids is a function of the localized concentration of plasma protein, principally albumen. Increasing the localized plasma protein concentration in the capillaries of the affected body segment results in an increase of the colloid osmotic pressure at those sites. By increasing the colloid osmotic pressure, plasma water extraction from the affected edemic interstitial spaces into the capillaries is also increased as is that in the peripheral veins. By removing plasma water from localized capillary circulation, over time, excess cellular water to the interstitial spaces is also removed and lymphatic drainage burden on the compromised lymphatic circulation is also relieved. By removing excess plasma water from the venous circulation immediately proximal to the affected edemic body segment, the systemic circulation and systemic body parts are not affected while edema in the body segment from which the plasma is removed is reduced.

In FIGS. **1** and **2** there is illustrated schematically the apparatus and treatment of the invention for reducing edema in a typical segmental body part, the left leg specifically referred to in FIG. **1**. However, it is to be understood that the principles of treating any other body segment, including either of a patient's legs, arms, peritoneal cavity, neck, etc. will apply, and that shown in FIG. **1** is for the purpose of illustration only. Accordingly, the iliac vein and femoral vein shown for inserting a plasma extraction device and a femoral artery for inserting a plasma protein return catheter are illustrative for treating edema in a person's leg. Although a femoral artery is illustrated in FIG. **1**, other arteries such as an iliac artery may be used instead for the return catheter. For example, when treating a patient's arms for edema, major veins useful for inserting the plasma extraction catheter may be the cephalic, auxiliary or basilic veins; major arteries for returning plasma protein which has been extracted include subclaviun, axillary and bronchial arteries. Again, it is to be understood that any major veins and arteries serving the edemic body segment to be treated according to the invention may be used.

Referring to FIGS. **1** and **2**, a hollow fiber plasma extraction element or device **12** affixed to the end of a plasma extraction catheter **13** is inserted in the iliac vein **11**. The design and structure of the hollow fiber extraction filter device is selected from filter elements and devices disclosed in the aforesaid patents. A preferred plasma filter device incorporates elongated hollow microporous fiber membranes as disclosed therein, and particularly a membrane having the morphology as disclosed in co-pending application Ser. No. 09/549,131, filed Apr. 13, 2000, the description of which is incorporated herein by reference. The specific location for insertion and placement of the hollow fiber extraction device will be in a major vein proximal to the subordinate veins that service the edemic tissues. Specific procedures for inserting the filter are understood by those skilled in the art. Plasma is diffused through the extraction element, and directed from the vein by convection as in the aforesaid patents using one or more positive displacement pumps **16** which operate along the extraction catheter. As illustrated, the extraction catheter **13** is preferably a dual lumen catheter having lumens **14** and **15**. A pressure sensor **18** may be located along the catheter, and where two lumens are present, the sensor may be used in one of the lumens, lumen **15**, whereby venous pressure may be periodically or selectively sensed by a microprocessor controller **30**. The microprocessor controller **30** also monitors other pressure sensors and is operational communication with the pumps as will be discussed further hereinafter. By sensing the pressure in the pressure sensors, the microprocessor controller **30** calibrates trans-membrane pressure and computes trans-membrane flux, thereby measuring the efficacy of the extraction membrane procedure.

The extracted plasma is directed to an ultrafiltration filter assembly **20** where plasma water is separated and removed from the extracted plasma fluid. The separated water is directed along plasma water line catheter **22** via pump **26** to plasma water waste container or bag **28**. A pressure sensor **24**, also monitored by microprocessor controller **30**, is provided in the plasma water line, and in response to the sensed pressure, pump **26** is operated by the microprocessor controller **30**. Thus, the rate of plasma water removed and separated is controlled by the monitored pressure sensors **18** and **24**, and pumps **16** and **26** are operated in response to the signals sensed by the microprocessor controller **30**. Parameters for operating the pumps in response to the sensed pressure are determined by a clinical protocol for treatment of the patient. The clinical protocol may be calculated based upon the degree of edema, in terms of the volume of fluid to be removed, and the acceptable rate of removal based on safe physiological transfer rates of fluids across the capillary bed and the measured osmolality of the arterial blood in the capillaries. The protocol may also take into consideration the practical amount of plasma water that can be removed while also providing adequate liquid remaining in the plasma protein fluid in order to be pumped by pump **32** for returning plasma proteins to the patient or to a protein collection container. As illustrated, after plasma water is separated from the plasma protein fluid in ultrafiltration apparatus **20**, the remaining fluid, which contains the desirable plasma proteins to be collected or returned to the patient, is directed via protein fluid line **35** to a protein collection container or bag **34** or to the patient via protein return catheter **40**. Pump **32**, also a positive displacement pump, is operated by microprocessor controller **30** in response to pressure sensed in pressure sensor **36**.

Either or both plasma extraction catheter **13** and protein return line **35** may be dual lumen catheters permitting fluid transfer from and to the blood as well as providing means of sampling both the venous and arterial blood for measurement of appropriate control parameters such as osmolality, hematocrit, and localized pressures. The plasma proteins separated from the plasma water separated in ultrafiltration filter **20** are directed to a protein collection container **34** and/or returned to the patient via protein return catheter **40**. The amount of protein returned to the patient may be selected for optimizing the capillary osmolality to a safe clinical protocol. For example a portion of the protein removed from the patient may be collected in a protein collection bag **34** and/or additional protein may be directed to the patient via a medicant syringe **42**. Thus, the apparatus and techniques of the invention provide for infusing more or less protein than is removed from the patient to meet the desired patient treatment. A medicant syringe **42** for infusing protein in the return line is illustrated cooperating with a 2-way stopcock **43** for infusing protein in the return line. The syringe may also be used for sampling plasma proteins in return catheter **40**. A pressure sensor **36** is also shown in the plasma return line cooperating with microprocessor controller **30** which monitors the pressure and, in response, selectively controls operation of pump **32**. Safety sensors **19** and **33** are also illustrated for detecting blood leaks in the extraction membrane assembly and/or a bubble detection sensor for detecting a leak in circuit tubing or components. The protein return catheter **40** is shown inserted in iliac artery **41**, by way of example, for treating a patient's leg for edema according to the invention.

The aforesaid system configuration is primarily designed for use in more advanced countries and medical facilities where medical and technical support and infrastructure is readily available with efficient and expert use for producing optimal clinical results in a desired period of time. The system illustrated in FIG. **3** is a somewhat simpler and relatively lower cost embodiment which may provide suitable treatment in areas or countries where the aforesaid medical and technical support is not readily available. In the system shown in FIG. **3**, a plasma extraction device **50** secured on a single lumen catheter **57** is inserted in a major vein **11** proximal to an affected edemic body segment. The plasma extraction device **50** utilizes ultrafiltration membranes rather than plasma filtration membranes used in the device in FIG. **2** and described above. Such an ultrafiltration membrane has a sieving coefficient and permeability cutoff such that only plasma water is extracted with a cutoff of approximately 2–3,000 daltons instead of plasma filtration membranes which have a cutoff of approximately 69,000 daltons. Thus, such an ultrafiltration filter device membrane has a pore size allowing only plasma water to be extracted and pass through the filter membrane. In the FIG. **3** apparatus the fluid extraction catheter **57** is connected to an ex-vivo siphon tube **59** for directing plasma water to a collection container **58**, for example, a graduated collection bag located approximately 1–2 feet vertically below the extraction element, thus providing a vacuum siphon means for extracting the fluid from the patient's circulation. The collection container **58** also provides means for monitoring the total fluid extracted during a specific therapeutic session. The extraction circuit shown includes a flow orifice **54** and check valve **56**. The extraction circuit also contains a mechanical vacuum gauge **55** for permitting the patient to monitor appropriate extraction rates and for adjusting or controlling the rate by raising or lowering the collection container or bag **58** relative to the extraction site, i.e., the location of plasma extraction device **50** in the major vein **11**. Another single lumen catheter **52** is inserted in an appropriate artery **51** proximal to the affected edemic body segment and is routed ex-vivo to an injection syringe **53** for providing means of injecting high molecular weight proteins into the capillary system of the edemic body segment, thereby raising osmotic pressure therein. Such increase in osmotic pressure is important in the resulting preferential extraction of plasma water from the edemic space. The injected protein may be blood bank albumen or other nutritious substance such as dextrose. Such features as well as operation of the apparatus illustrated and the advantages thereof for treating segmental edema according to the invention will be evident to those skilled in the art.

What is claimed is:

1. A method of treating segmental edema in a patient comprising:

inserting a plasma extraction device in a major vein proximal to a body segment containing edemic tissue, said plasma extraction device comprising a plasma extraction filter capable of separating plasma including plasma proteins from blood in-vivo within said vein and a plasma extraction catheter for directing separated plasma from the plasma extraction filter to an ultrafiltration apparatus;

inserting a return catheter in a major artery of the body segment from which the plasma is extracted;

separating and extracting plasma and plasma proteins from blood in the major vein through said plasma extraction filter;

directing the extracted plasma through the plasma extraction catheter to an ultrafiltration apparatus and separating plasma water from plasma proteins therein, and collecting and/or discarding the separated plasma water; and

directing plasma proteins via the return catheter to the major artery of the body segment of the patient from which the plasma is extracted.

2. The method of claim **1** including directing separated plasma water from the ultrafiltration apparatus to a collection container via a plasma water line.

3. The method of claim **1** comprising pumping extracted plasma from the plasma extraction filter to the ultrafiltration apparatus.

4. The method of claim **2** comprising pumping extracted plasma from the plasma extraction filter to the ultrafiltration apparatus.

5. The method of claim **1**, **2**, **3** or **4** comprising pumping plasma proteins from the ultrafiltration apparatus to the major artery.

6. The method of claim **5** comprising pumping plasma water from the ultrafiltration apparatus to a collection container.

7. The method of claim **5** including sensing pressure in the plasma extraction catheter and the plasma water line and in response thereto controlling the amount and rate of plasma extraction and plasma water separation.

8. The method of claim **7** comprising controlling the pumping of the extracted plasma and separated plasma water in response to pressure sensed in the plasma extraction catheter and plasma water line.

9. The method of claim **7** including directing amounts of plasma proteins to the patient via the return catheter different than amounts extracted through the plasma extraction filter.

10. The method of claim **5** including directing amounts of plasma proteins to the patient via the return catheter different than amounts extracted through the plasma extraction filter.

11. The method of claim **10** wherein at least a portion of the plasma protein extracted from the patient is returned to the patient.

12. The method of claim **1**, **2** **3** or **4** comprising pumping plasma water from the ultrafiltration apparatus to a collection container.

13. The method of claim **1** including sensing pressure in the plasma extraction catheter.

14. The method of claim **1** including selectively directing separated plasma proteins to a collection container.

15. The method of claim **1** wherein at least a portion of the plasma protein extracted from the patient is returned to the patient.

16. The method of claim **1** wherein the plasma extraction device is inserted in the iliac or femoral vein and the return catheter is inserted in the iliac or femoral artery.

17. A method of treating segmental edema in a patent comprising:

inserting a plasma water extraction device in a major vein proximal to a body segment containing edemic tissue, said plasma water extraction device comprising an ultrafiltration membrane capable of separating plasma water from blood and plasma protein in-vivo within said vein and a plasma water extraction catheter for directing separated plasma water from the plasma water extraction membrane;

inserting a return catheter in a major artery of the body segment from which the plasma water is extracted;

separating plasma water from blood in-vivo in the major vein through said ultrafiltration membrane and directing the separated plasma water from the vein via the plasma water extraction catheter to a plasma water container; and

directing plasma protein via the return catheter to the major artery of the body segment of the patient from which the plasma water is extracted.

18. The method of claim **17** wherein the location of the inserted plasma water extraction device is elevated relative to the position of the plasma water container, wherein the method includes:

observing the rate of plasma water collected in the plasma water container and adjusting or controlling the rate by raising or lowering the container relative to the plasma extraction device.

* * * * *